

Non-Technical Abstract

We have developed a method of delivering genes specifically to tumor cells, both primary tumor and metastatic disease, through the blood stream. This method entails the use of a lipid molecule (liposome) surrounding a plasmid DNA that codes for the specific therapeutic gene. Coating the surface of this lipid-DNA is a protein molecule that will bind to the transferrin receptor, which is present at high levels on most tumor cells, an anti-transferrin receptor single-chain antibody fragment. We have also found that the complex is stable for up to six months at 4°C after freeze-drying. One of the genes we will deliver is the normal human p53 gene, the function of which is to control cell growth and allow cells to die if they are too damaged by radiation or chemotherapy. This gene is abnormal in ~60% of human tumors. Restoring a normal copy of this gene to the cancer cells will make them respond better to standard radiation or chemotherapy. The second gene being delivered by this complex is RB94, also a tumor suppressor gene. RB94 is a modified form of the retinoblastoma tumor suppressor gene but with enhanced tumor cell killing ability and no effect on normal human cells.

Pre-clinical studies indicated that these complexes have low toxicity. More importantly, intravenous treatment of mice carrying human tumor xenografts with these complexes resulted in significant tumor growth inhibition.

We propose to perform separate clinical trials of the complexes carrying either the normal p53 or RB94 gene to first test for safety (alone or in combination with standard therapies) and then for effectiveness against cancer. The trials with p53 will be performed at the Lombardi Cancer Center at Georgetown University, Washington DC, while the RB94 trials will be at the M.D. Anderson Cancer Center, Houston, TX.